Face value

van der Gaag, Christiaan Michiel

Chapter 1

Pre-Face

A man's face as a rule says more, and more interesting things, than his mouth, for it is a compendium of everything his mouth will ever say, in that it is the monogram of all this man's thoughts and aspirations.

Arthur Schopenhauer (Parerga and Paralipomena, vol. 2)

"The psychiatrist felt a sudden rush through his body, his heart started to beat faster, his breathing rhythm increased and his face intensified. He had just looked at his morning schedule and saw the name of the next patient. Immediately he remembered the intake meeting he had with his colleagues who updated him on the latest aggressive behavior of the patient he had just seen once briefly during a supervised intake. He still remembered the outlines of the patient's face with small eyes looking nervously at his surroundings. The broad nose was colored reddish with several skin imperfections reflecting past adolescent acne problems. The mouth was outlined sharply, lips clenched, unwilling to speak. The patient had seemed anxious that time, although the psychiatrist was not sure about the exact reason of the patients' discomfort. The tension of the patient had had its impact on the psychiatrist, as he had felt some anxiety himself. He thought about the violent spells of this patient, that his colleagues spoke about, and was not looking forward to the consultation. His task was to propose the reluctant patient medication for his hyperactivity. No simple task, as the patient had refused it convincingly during the intake procedure. Still thinking about how to handle the case, the psychiatrist went to the waiting area to pick up the patient. The patient and psychiatrist recognized each other, after which the patient started to show a smile on his face. This surprised the psychiatrist as he had not seen a single smile during their first meeting. Consequently, the psychiatrist felt some relief in his body. He started to relax and replied almost automatically with a similar smile… After shaking hands they both walked a little lighter towards the consultation room".

The significance of faces

It is hard to overestimate the importance of faces in daily life. First of all, they are central for identity recognition. Thanks to this face-based identification, we can attribute all kinds of knowledge acquired through personal experiences with people or through verbal knowledge communicated by other people. Relatives, friends, colleagues and acquaintances get 'coloured' by this process, and become personalities, thereby changing their significance for us. Second, faces have an important communicative function (Blair, 2003). For example, they can display emotional feelings or transmit messages in the form of facial expressions, show intentions, aid in the understanding of speech. Expressions contain both a sending aspect and a receptive side. Through the *sending* aspect we can transmit all kinds of daily life messages to specific persons: showing your child that he should not have touched the precious vase, showing your partner that you liked him cleaning the bathroom, showing friends that this piece of maggot-infested Sardinian cheese is disgusting, and so on. Faces can therefore contain reinforcer-messages to modulate the target behaviour of the receiver in the future (Blair, 2003; Russell et al., 2003). The *receptive* side is important for the opportunity faces give in understanding what goes on in a fellow-human being. This last process often occurs effortlessly, particularly with people we are close to. We can even feel what someone else is feeling based on facial expressions, the process of which has been called 'empathy'.

Furthermore, evolutionary theorists assume that faces have survival value. An example are disgusted faces, which can transmit a message like: 'don't eat this maggot infested Sardinian cheese, you might become sick or die from it'. So your friends' faces might warn you, prevent you from tasting bad substances, and limit illnesses or worse (Rozin et al., 1993). This aids in survival of the species in general and of one person in particular, you. However, faces might exaggerate: in the case of the Sardinian cheese, the maggots are essential to it. Your friends' disgusted faces can thus also prevent you from experiencing a fine Sardinian delicacy: Formaggio marcio. Faces can therefore also be instruments of deception.

Facial expressions have a professional aspect as well. In psychiatry for instance, the lack of facial expressions of a patient might aid in diagnosing disorders like autism and schizophrenia (American Psychiatric Association, 2000; Lord et al., 1989; Berenbaum and Oltmanns, 1992). On the other hand, facial expressions performed by a psychiatrist might encourage patients to share their feelings and cognitions during an intake procedure (Shea, 1988). Moreover, in psychotherapy sessions, a therapist can show congruent facial behaviour in line with that of the patient, either consciously or unconsciously (facial mimicry or the 'chameleon-effect') (Chartrand and Bargh, 1999). Mimicry facilitates the smoothness of interactions and increases liking between interaction partners (Chartrand and Bargh, 1999), which in the case of psychotherapy might tighten the therapist-patient relationship. This relationship can be classified as a non-specific therapy factor, in that it is shared by most forms of psychotherapy. Importantly, non-specific therapy factors have been shown to be of particular importance in therapy outcome studies (e.g. Luborsky et al., 1985; Krupnick et al., 1996; Horvath and Luborsky, 1993), even in psychopharmacology interventions (Krupnick et al., 1996). The face might also be a mediator in psychotherapy, for instance during exposure sessions of cognitive and behavioural therapy, when posing in a specific bodily posture and congruent facial expression might induce cognitive, affective and/or behavioural change (Camras et al., 1993).

Everybody in society has first-hand experiences with faces, which makes them important stimuli for research into social processes. Combining the interest in our social nature, our universal experience with faces as fundamental building blocks of our 'socialness', and our realization that the brain is the processing site of our senses, it is not surprising that a major goal of social science was and is to understand face processing in the brain. Early evidence existed that the brain contained specialized regions and neurons dedicated for the processing of faces. In humans, it had been shown that lesions in a brain area called the temporal cortex lead to a disorder named prosopagnosia, the selective inability to recognize other people through the sight of their faces (Meadows, 1974; Bruyer et al., 1983; Tranel et al., 1988; Damasio et al., 1982). In the monkey, cells were found in distinct regions of the temporal cortex that specifically responded to images of faces (Gross et al., 1972; Rolls et al., 1977; Perrett et al., 1982). Moreover, it was shown that some of these cells were particularly tuned towards facial identity (Yamane et al., 1988), facial expressions (Hasselmo et al., 1989) or viewpoint (Perrett et al., 1991). The development of neuroimaging techniques from the early 90s on, enabled scientists to investigate the neural underpinnings of face processing in humans non-invasively. In the present thesis, a neuroimaging technique called functional magnetic resonance imaging (fMRI) was used to study face processing in humans. First, I will very briefly describe fMRI, then I will sketch some of our current concepts in facial processing in the human brain, after which I will describe some models of facial expression recognition and production. Finally, I will outline some clinical implications and the research questions of this thesis.

Functional Magnetic resonance Imaging (fMRI)

Neuroimaging of functional activation relies on the assumption that brain function (neural activity) can be described by measuring perfusion related phenomena that are changed by neuronal activity. Functional MRI (fMRI) is a non-invasive imaging technique for acquiring spatiotemporal information about the brain and other organs (Kwong et al., 1992; Ogawa et al., 1992). It can be tuned to a variety of physiological parameters, but in general the signal is dependent upon cerebral blood flow (CBF), cerebral blood volume and blood oxygenation. The T2* or blood-oxygenation-level-dependent (BOLD) fMRI signal is primarily, as the name suggests, sensitive to blood oxygenation.

When the oxygen demand of neuronal tissue increases (e.g. by means of an increased neuronal firing rate), the rate of delivery of oxygen to the neuronal tissue, via increases in CBF and blood volume, outstrips the rate of oxygen extraction. The result is an *increase* in oxygenated hemoglobin in the venous pool. Oxygenated hemoglobin is diamagnetic; it does not have an intrinsic magnetic orientation. However, deoxyhemoglobin is paramagnetic and the resultant decrease in deoxyhemoglobin in the venous pool is associated with an augmentation in the BOLD signal (so called 'activations') during fMRI data acquisition (see e.g. Logothetis, 2003 for a review). Despite its wide application in neuroscience, only recently it has been shown that the BOLD response directly reflects neural activity (Logothetis et al., 2001; Hyder et al., 2002; Smith et al., 2002).

An fMRI experiment consists at least of two conditions, one condition of interest and one control condition. In order to get the most straightforward explanations from the results of fMRI experiments, the two implemented conditions should differ only in one feature or function of interest. The neural activity associated with this feature or function can be implied after comparing the two conditions (subtraction method).

Processing of facial expressions in the brain

Face Perception

In the most influential neuro-anatomical model of face perception of these days (Haxby et al., 2000a; Haxby et al., 2002; Gobbini and Haxby, 2006), the processing of facial identity and facial expression are hypothesized to be taking place in distinct brain regions (Figure 1), analogous to face-processing in monkeys described before. Invariant aspects of faces, like people's identities, are thought to be processed through the lateral fusiform gyrus, while changeable aspects of faces, like facial expressions, might rely more on the superior temporal sulcus (STS). Since the lateral fusiform gyrus has a preference to process faces over other object categories ('face-specificity') (Kanwisher et al., 1997; Yovel and Kanwisher, 2004), this region has been dubbed the 'fusiform face area' (FFA) (Kanwisher et al., 1997). A bilateral lesion of the FFA is the most common cause of prosopagnosia (Damasio et al., 1982). The nature of lateral fusiform gyrus and STS activations is unclear, although some theories suggest that activations in the lateral fusiform gyrus reflect processing of facial form, while activations in the STS reflect stored information about biological motion that is needed to identify facial expressions (Chao et al., 2002; Tsunoda et al., 2001).

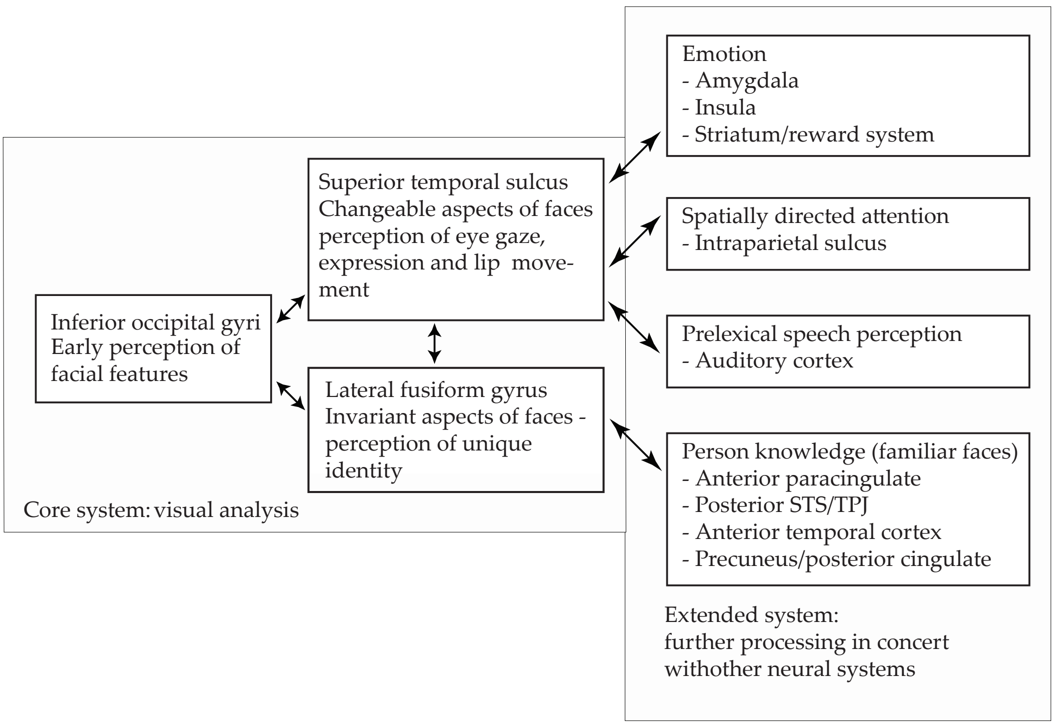

Figure 1: Face perception model after Haxby et al. (2000, 2002) and Gobbini & Haxby (2007). For discussion see main text. STS=superior temporal sulcus; TPJ=temporo-parietal junction

Furthermore, the model divides face processing regions into a core system specialized in face processing, including both the lateral fusiform gyrus and the STS, and an extended system, consisting of regions that participate in related cognitive functions (Figure 1). Regions of both the core and the extended system interact to mediate the processing of identity, facial expression, speech-related mouth movements and the spatial focus of another's attention. A more recent version of the model describes the distributed set of areas that process *familiar* face recognition (Gobbini and Haxby, 2006), adding brain structures that participate in the retrieval of person knowledge and social semantics (meaning of faces in the social domain), such as personality traits, mental states and intentions. Figure 1 is a merged version of both models, while Figure 2 displays the anatomical location of the majority of the brain regions mentioned in the model (and other brain regions discussed later). Summarizing the model, the core system processes the visual features of faces, while the extended system is all about giving meaning to faces and associated features and functions. The extended system involves those brain circuits that recognize the person next to you as being your friend, that recognize his disgusted facial expression during Formaggio marcio tasting, that aid in understanding the accompanying 'that's disgusting!' outcry, and that help you in remembering that your friend sometimes is a bit of a drama queen. People get significance, valence and meaning based on processes taking part in the extended system, they become individuals important for our daily life social interactions.

However, the descriptions of both the core and extended system appear to be oversimplifications of face processing in the brain. In the case of the core system, the clear separation between identity recognition and facial expression processing might be partially a theoretical separation (see Calder and Young, 2005 for a review). Next, besides the lateral fusiform gyrus, multiple patches of cortex in the ventral visual processing stream are more responsive to faces as compared to other visual object categories (Haxby et al., 2001; Spiridon and Kanwisher, 2002). In the case of the extended system, it is still largely unknown what brain circuits compose this system and what the contribution is of participating brain areas.

It is important to note that other neuro-anatomical models of face processing exist (Adolphs, 2002). However, the overarching topic of this thesis is the attribution of meaning to faces, which involves both identity processing and expression processing. Identity processing is not part of the model by Adolphs, therefore Haxby's model was chosen.

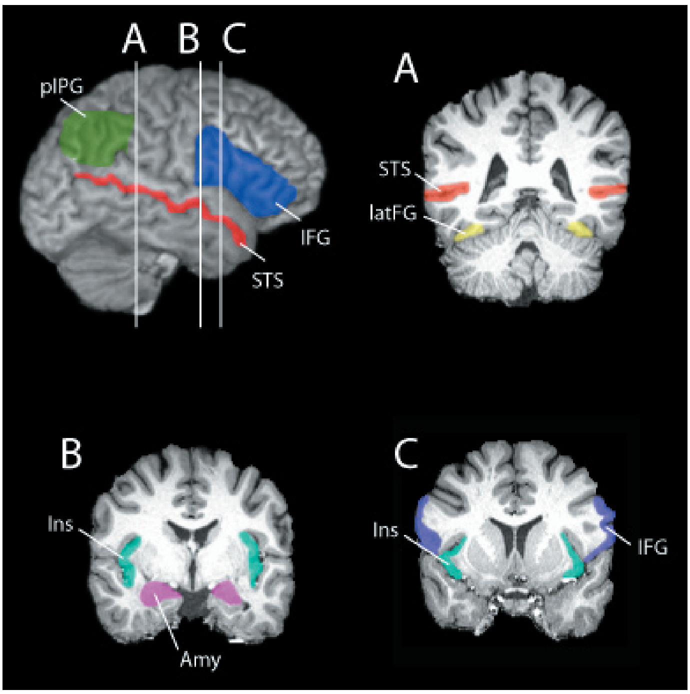

Figure 2: Brain regions central in face perception, as outlined and studied in this thesis. Upper left: typical MRI-image of the right side of the brain, displaying several brain regions important in face perception. Locations of the coronal sections in A, B and C are shown. Amy=amygdala; IFG=inferior frontal gyrus; Ins=insula; latFG=lateral fusiform gyrus; pIPG=posterior inferior parietal gyrus; STS=superior temporal sulcus.

Production of facial expressions

The classical picture of (cortical) motor control of facial expressions is similar to that of the motor control of arm or muscle movements: voluntary movements are being executed by the primary motor cortex, which is located on the lateral surface of the brain (M1) (see figure 3). Neurons from M1 project to the facial nucleus in the brainstem, which forms the neuroanatomical basis of the n. facialis. The n. facialis directly controls the vast majority of the facial muscles that together orchestrate all facial movements, including facial expressions. The planning of the actual movements is controlled by both the premotor cortex (PM) and the supplementary motor area (SMA), located on the lateral and medial surface of the brain, respectively. Selection and preparation might be a function of the pre-supplementary motor area (pre-SMA), located rostral to the SMA. However, neuroimaging, neuroanatomical and patient studies have led to a more refined picture of motor control of facial expressions. First, motor control of facial expressions seems to be more complex, in that additional cortical brain regions take part in the execution of facial expressions. Next to the already mentioned regions and several subcortical regions (Hopf et al., 1992; Hopf et al., 2000; Urban et al., 1998), it has been shown in monkeys that two locations of the cingulate cortex (CZa and CZp) have direct projections to the facial nucleus in the brainstem (Morecraft et al., 2001). This organizational pattern might be similar in humans (Picard and Strick, 1996; Picard and Strick, 2001). Second, involved brain regions might contribute differentially to the execution of facial expressions, in that the M1, premotor cortex and the CZa are relatively more involved in movements of the lower facial region, while the SMA and CZp control more substantially upper facial movements (Morecraft et al., 2001; Morecraft et al., 2004). Third, volitional and spontaneous emotional movements might be under the control of distinct components of the circuit described before (Weller, 1993; Hopf et al., 1992; Sim et al., 2005).

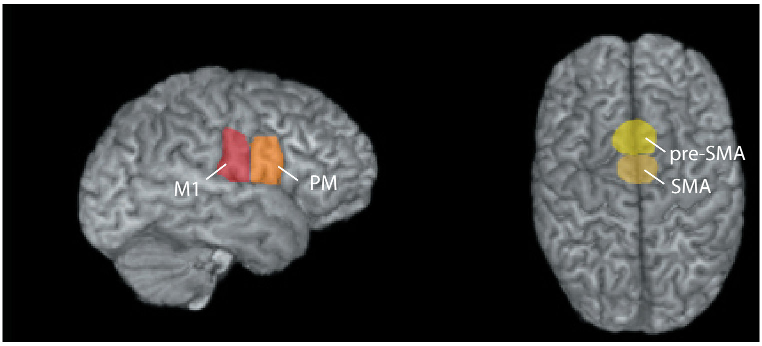

Figure 3: Several brain regions central in facial expression production, as outlined and studied in this thesis. Left: typical MRI-image of the right side of the brain. Right: typical MRI image of the brain from above. M1=primary motorcortex; PM=premotor cortex; SMA=supplementary motor area; pre-SMA=pre-supplementary motor area.

Facial expression theories

Facial expressions are very important in the large amount of social encounters we have daily. People that can not produce or have difficulties reading facial expressions can have severe problems in social functioning. The everyday struggle of these people has been intriguingly described in a book by Jonathan Cole, with personal accounts of people that are congenitally blind, have Möbius Syndrome (neurological condition in which patients cannot move their facial musculature) or have autism (Cole, 1999). But what do facial expressions actually express? Different models exist, several of which will be briefly outlined:

1. Discrete emotion theories (Ekman, 1992; Panksepp, 1998; Tomkins, 1962): these theories posit that emotions can be divided into discrete categories. Each individual emotion is unique in its physiological, behavioural and psychological manifestations, which are the result of unique activations within the (central) nervous system. This influential model is based on Darwin (1872), who posited that existing (basic) emotions are globally encountered, are developed and selected through evolution and are genetically inherited. Darwin's model is supported by behavioural studies which have shown that around the world in all cultures, a small fixed number of discrete emotions exist (Ekman et al., 1987; Ekman, 1994). They are called the basic emotions, and consist of: happy, surprise, sad, disgust, angry and fear. Tomkins (1962) argues that each genetically encoded basic emotion can vary in intensity and consists of a single brain process (an 'affect program'). Specific eliciting conditions can automatically activate a distinct affect program, thereby generating all the various signs of that specific emotion, including its corresponding facial and vocal expression, autonomic changes, subjective experience and instrumental action. Moreover, these different basic emotions are thought to be decoded and recognized by distinct brain regions. Recently, discrete emotion theories increasingly encounter criticism. For instance, these theories

can not explain the clinical observation of high comorbidity rates of anxiety and mood disorders and they are incompatible with findings from the fields of genetics and temperament (Posner et al., 2005). Moreover, the existence of universal basic emotions has been questioned (e.g. Turner and Ortony, 1992; Russell and Fernandez-Dols, 1997). Given these shortcomings, several researchers developed alternative models and proposed a conceptual shift in the theory to study emotion.

2. Dimensional models (e.g. Russell et al., 2003; Watson et al., 1999; Posner et al., 2005): in general, dimensional models of emotions presume that all affective states are the end product of common, overlapping neurophysiological systems. One of these models, the circumplex model, proposes that two neurophysiological systems mediate all affective states: a valence system (pleasure-displeasure continuum) and an arousal or alerting system. Each emotion, with corresponding facial expression, can be understood as a combination of varying degrees of valence and arousal. In addition, cognitive processes appraise situations based on salient aspects of the environment and memorised past experiences (Posner et al., 2005). This model excludes the existence of distinct individual emotions with their individual CNS hardware. The value of the circumplex model lies in the fact that it can offer novel experimental paradigms for future neuroimaging, genetic and clinical studies (Posner et al., 2005).

3. Componential emotional model (e.g. Scherer and Ellgring, 2007): according to this model, facial expressions display distinct *components* of the emotion process, which are patterned by the results of a sequential appraisal process. In short, each witnessed experience is being evaluated by an appraisal *sequence* (1, relevance of an event; 2, implications for major needs and goals; 3, ability to deal with these consequences; 4, normative significance of the event), the end product of which is a wide variety of complexly patterned emotional episodes. The resulting facial expression can be predicted, based on assumptions of facial movement outcomes of the distinct appraisal events and characteristics of modal emotions. So, this model assumes that a variety of facial expressions exist, including some modal emotions.

However, the vast majority of existing neuroimaging and neuropsychological experiments on facial expressions implemented basic facial expressions and found some categorical effects (e.g. Phillips et al., 1997; Calder et al., 2001). To be able to compare our findings with the existing literature, we adopted, despite its shortcomings, the model of the discrete emotion theory. This theoretical choice will be evaluated in the discussion of this thesis.

Thesis outline

The present thesis is about refining our understanding of the brain areas that underlie the extended system, the neural circuits involved in the attribution of meaning to persons in our environment. We will particularly focus our attention on the processing of facial expressions and social semantics. I will discuss in the next section some limitations of the model by (Haxby et al., 2000a; Haxby et al., 2002; Gobbini and Haxby, 2006) centered around facial expressions and social semantics, which will be addressed in the studies described in the upcoming chapters of this thesis. Based on results of the investigations, I will recommend in the general discussion (chapter 7) some adaptations of the model presented in Figure 1.

One important *function* of the attribution of meaning to faces is the recognition of facial expressions. The model proposes that the STS would mediate facial expression recognition in combination with regions in the extended system, especially the amygdala. A classic paradigm that investigates facial expression processing involves the comparison of emotional faces with faces containing a neutral expression. Importantly, this paradigm is based on the discrete emotion theory mentioned previously. The first wave of studies reported that the amygdala responded selectively to the sight of negative emotions, fear in particular (Phan et al., 2002). Without amygdalae, people are thought to be impaired in their capacity to recognize fear in others (Adolphs et al., 1994). This view has been engraved into the mind of many a psychologist, neurologist and neuroscientist for years. Recently, the fear-specificity hypothesis of the amygdala has been challenged. In a pivotal paper, Adolphs et al. (2005) surprisingly showed that a patient with bilateral amygdala lesions is quite capable of recognizing fear, if only she is forced to look at the eyes of the photographs she has to rate. This finding suggests that the amygdala per se is not fear selective, but 'simply' helps in processing faces by biasing the viewer to the eye region. Almost at the same time, Paton et al. (2006) published a paper showing that the amygdala also contains neurons selective for the positive valence of visual stimuli, with these positive-valence neurons being as frequent as the negative-valence counterparts, supporting the idea that the amygdala can no longer be seen as a negative valence processor. Functional neuroimaging data to support this conclusion would be crucial in providing a strong foundation for the development of a new understanding of the function of the amygdala.

Under ecological circumstances facial expressions are dynamic displays. However, almost all published studies used static facial photographs to study the fear specificity of the amygdala. A switch from using movies instead of static displays will capture the dynamic nature of facial expressions. Consequently, it could substantially increase the ecological validity of neuroimaging experiments (Adolphs, 2002; Russell et al., 2003). An experiment testing the amygdala with fearful movies contrasted against another negative (e.g. disgust) and a positive emotion (e.g. happiness) would allow to assess the amygdalar's putative selectivity for fear. Unfortunately, this critical test has not been performed so far. In chapter 2, we will report our study on the fear selectivity of the amygdala using dynamic displays.

A promising *process* that might be important in the understanding of the actions of other people (including facial expressions) is 'simulation' (Adolphs, 2002; Carr et al., 2003; Goldman and Sripada, 2005; Keysers and Gazzola, 2006). In case of witnessing a facial expression, simulation might spontaneously trigger in the observer representations of the motor program of the observed facial expression and/or the emotional program that defines the underlying emotion. These processes might put you, figuratively speaking, in the shoes of the observant and aid in the understanding of facial expressions and intentions of other people. Haxby's model does not take recent studies into account that reported evidence of the existence of simulation mechanisms in the brain during the recognition of facial expressions (Adolphs et al., 2000; Pourtois et al., 2004; Heberlein et al., 2004; Wicker et al., 2003; Jabbi et al., 2007). Lesion and TMS studies support the idea that emotion recognition is mediated by a simulation mechanism within the observer's somatosensory cortex, as if the observer would feel similar emotional states as the person being observed. In particular, the understanding of facial expressions has been studied through the mirror neuron system (MNS). The critical property of this system is that the observation of a particular action of another person activates regions involved in the execution of that particular action, which is a form of simulation (Goldman and Sripada, 2005). This explains the term 'mirror' neuron, the neuron 'mirrors' the behavior of another person, as though the observer was performing the action. Given it's combined role in action perception *and* action execution, the mirror neuron system is theorized and believed to be involved in functions like action understanding, empathy and imitation (Rizzolatti et al., 2001; Rizzolatti and Craighero, 2004; Keysers and Gazzola, 2006; Iacoboni et al., 1999; Wohlschlager and Bekkering, 2002; Heiser et al., 2003). Both in monkeys and humans, a vast literature exists describing the classical MNS to be composed of the posterior parietal cortex and the premotor cortex (Brodmann Area (BA) 6 and 44)[1] (e.g. Rizzolatti et al., 2001; Rizzolatti and Craighero, 2004). The superior temporal sulcus (STS) is closely related to the classical mirror neuron system in terms of function and connections but lacking clear motor

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[1] *The nomenclature of inferior frontal brain regions is quite complicated. Based on brain morphology, the frontal cortex is divided in an inferior, medial and superior frontal gyrus. In addition, the posterior half of the IFG is subdivided in a pars triangularis and a pars opercularis (Tomaiuolo et al., 1999). Given it's function in motor planning, part of the inferior frontal gyrus (IFG) has been named the premotor cortex. Citoarchitectonic studies after Brodmann (Brodmann, 1909), separated part of the IFG in BA44 and BA45. Together, BA44 and BA45 in the left hemisphere have been named Broca's area, after Paul Broca, who described the importance of the left IFG in language functioning (Broca, 1865). In the present thesis, we will follow the nomenclature tradition of the different topics that are discussed. Unfortunately, this will sometimes result in somewhat confusing discussions.*

properties (Keysers and Gazzola, 2006) (see Figure 2 and 3 for locations of these brain areas). Interestingly, BA 44 constitutes in combination with BA45 Broca's area, which has been shown since it's first description by the French neurologist Paul Broca in 1865 to be important in language function (Broca, 1865). This anatomical overlap of a brain area crucial for language functioning with the location of mirror neurons that are thought to be important for action understanding and imitation, has tempted many a scientists to speculate on the significant role of mirror neurons in language development and functioning (Rizzolatti and Arbib, 1998; Arbib, 2005; Fadiga and Craighero, 2006; van Schie et al., 2006; Iacoboni and Wilson, 2006).

The MNS might also be involved in the understanding of facial expressions, since several neuroimaging studies showed that the premotor and parietal cortex were both involved in facial expression observation *and* execution (Carr et al., 2003; Leslie et al., 2004; Hennenlotter et al., 2005). In addition, Carr et al. (2003) showed that two regions that are important for emotion processing, the amygdala and insula (see Figure 2), were also involved in the observation and execution of facial expressions. The insula was also found to be activated in a study where subjects had to observe *and* experience the emotion 'disgust' (Wicker et al., 2003). These findings support the idea that, besides a MNS for actions, there exists a MNS for emotional states. The emotion specificity of the MNS has not been studied so far. One fMRI study mixed different emotions within presentation blocks (fear, disgust, happy, sad, angry, surprise), therefore making comparisons between facial expressions impossible (Carr et al., 2003). The only study which investigated multiple emotions *separately* (disgust and pleasure) was performed by Wicker et al. (2003), although they only studied one positive and one negative emotion. A region activated in both these studies was the anterior insula, which has been theorized to particularly process disgust (Calder et al., 2000; Calder et al., 2001). It is still unclear whether the anterior insula activation found by Carr et al. (2003) mentioned before is specifically related to disgust processing or whether it is involved in the processing of multiple emotions. The same discussion stands for the amygdala, another brain region activated in both facial expression observation and execution in the study from Carr et al. Data from animal studies and lesion patients have shown the importance of this structure in particularly the processing of fear (LeDoux, 2000; Calder et al., 2001; Adolphs et al., 1999), however see (Adolphs et al., 2005). The amygdala activations in the Carr study could therefore be exclusively related to fear processing, as their paradigm included fearful expressions as well. In summary, it is still uncertain if individual emotional facial expressions are treated differently and/or specifically within the motor and/or 'emotional' MNS. We will investigate this question in the present thesis.

The attribution of personality traits to people also gives faces additional meaning. In the model by Haxby et al. (figure 2), the social semantics system (meaning of faces in the social domain, e.g. personality traits) is placed outside the core system of facial perception, while there is some evidence that the lateral fusiform gyrus/FFA might be involved in social functioning outside of face perception, e.g. during social semantic processing (Castelli et al., 2000). Studying brain activations during the passive observation of movies containing interacting geometric shapes that strongly suggested agency (Heider and Simmel, 1944), Castelli et al. reported the involvement of the lateral fusiform gyrus. This activation was unexpected, as the stimuli did not contain pictures of faces. Although the localization of the fusiform activations in their study is in the area generally reported to be the FFA, it is not clear whether this region of activation would have overlapped with the FFA in these subjects, as no FFA localizer task was performed (Saxe et al., 2006). FFA localizer tasks are necessary, as the location of the FFA can vary from subject to subject. In addition, a brain region which has been implicated in social information processing is the left inferior frontal gyrus (IFG). Lesion data have shown the importance of this region in emotional (Adolphs et al., 2000) and personality trait attribution (Heberlein et al., 2004; Heberlein and Saxe, 2005). However, IFG activations are difficult to interpret, since the IFG has been reported to be involved in a wide variety of functions, including language (Poldrack et al., 1999), action understanding (Rizzolatti et al., 2001) and executive functioning (Collette et al., 2006). In conclusion, despite limited available evidence, it is uncertain whether the FFA is involved in social functioning outside basic face perception processing, and if so, whether this additional function might be of a social semantic nature. Social semantics might also rely on the IFG, although the available evidence is limited. These issues will be addressed in this thesis.

Clinical implications

Although this thesis has no direct clinical implications, the study of face processing is important given the significance of this function in our daily lives, as outlined above. Moreover, it might have a contribution to the understanding of psychiatric disorders known for their social deficits (including the aberrant processing of faces), e.g. autism and schizophrenia. Autism is a severe developmental disorder and is defined by a triad of symptom domains: stereotyped behaviors and interests, communication disturbances and social deficits (American Psychiatric Association, 2000). A striking feature of autistic individuals is that they appear not to share the emotions of others in an automatic and intuitive way. They do not spontaneously feel what someone else is feeling based on facial expressions, and, consequently, appear less empathic. The way people with autism attribute meaning to faces seems different from non-autistic people, which is reflected by possible aberrant face processing in the brain (Schultz et al., 2000a; Critchley et al., 2000b; Pierce et al., 2001; Hubl et al., 2003; Dapretto et al., 2006; however see Pierce et al., 2004; Hadjikhani et al., 2004). By identifying the neural circuits normally involved in sharing the emotions of others, and investigating if autistic subjects show abnormal activity in these face and emotion processing circuits, we could gain insights into the very core of their social deficits. Schizophrenia is a psychotic disorder in which the patient also suffers from social deficits, in combination with distorted thinking, hallucinations and/or a flattening of affect (American Psychiatric Association, 2000). Like autism subjects, schizophrenia patients have difficulties in the recognition of facial expressions and deficits in emotional experience and regulation (Edwards et al., 2002; Aleman and David, 2006; 't Wout et al., 2007). The original aim of my PhD project was to study the social deficits of autism by comparing them with two control groups, healthy controls and schizophrenia patients. Therefore, in a combined effort with investigators from Accare, the BCN Neuroimaging Center and the GGZ-Drenthe, we developed an ambitious research protocol (included in the present thesis as an appendix). Unfortunately, due to time constrains, I could not execute the protocol myself. Luckily, this project will be carried out by my adherent at the BCN Neuroimaging Center, Jojanneke Bastiaansen.

Research questions of the present thesis

In investigating the neural mechanisms of the social meaning of faces, we came to the following main research questions:

1 *The function of the amygdala in the processing of facial expressions (Chapter 2)*

Is the amygdala selective for fear processing under more ecological conditions, i.e. by using movies of facial expressions instead of static photographs?

2 *Understanding of facial expressions through the mirror neuron system (MNS) (Chapter 3)* a) Does the MNS become spontaneously active when observing facial expressions, even when subjects do not need to execute facial expressions? b) Are the individual emotional facial expressions treated differently and/or specifically within the classical MNS? c) Are the involvement of the insula and the amygdala during facial expression observation and production emotion specific?

3 *Social cognition and the fusiform face area (FFA) (Chapter 4)* Does the role of the FFA in social

processing proceed beyond the ‘simple’ processing of visual aspects of faces?

4 *Social semantics involvement of the FFA and IFG (Chapter 5)* Are the FFA and IFG involved in the processing of third-party acquired social semantics related to faces?

5 *Autism and the MNS (Appendix)* How can social deficits in autism be studied within the framework of the MNS using fMRI?